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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/992,840	11/06/2001	Michael E. Jeffers	15966-557A (Cura 57A)	7261

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EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	PAPER NUMBER
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/992,840	JEFFERS ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon, Ph.D	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2006 and 16 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *39-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/18/02, 10/18/02 & 7/17/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group I, claims 1-38 drawn to a method of promoting the growth of a population of cells or treating an inflammatory pathology comprising contacting at least one cell with a protein composition in response filed on 9/14/06 is acknowledged. In addition, Applicant has also elected SEQ ID NO: 2 with traverse. Applicant requests that the Office in addition to SEQ ID NO: 2 should search SEQ ID Nos: 4, 6, 8, 10, 12 and 14 because SEQ ID Nos: 4, 6, 8, 10, 12 and 14 are all drawn to FCTRX polypeptides and share significant sequence identity. This argument is found to be persuasive. Therefore, SEQ ID Nos: 2, 4, 6, 8, 10, 12 and 14 will all be searched. The Office also acknowledges the submission of the sequence on 1/16/2007.

Claims 1-48 are pending. Claims 39-45 are withdrawn as being drawn to unelected inventions. Claims 1, 4, 5, 6, 9, 10, 17, 20, 21, 28, 31 and are 32 have been amended. Therefore, claims 1-38 will be examined.

Drawings

2. The drawings filed 11/06/2001 are acknowledged.

Information Disclosure Statement

3. The IDS's submitted on 7/18/2002, 10/18/2002 and 7/17/2003 have been considered.

Specification

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

5. Applicant is required to update the priority information by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

6. Please check the specification for typographical errors (for example, page 115, line 13, clone as been misspelled cline).

7. The use of the trademark Cremophor EL, Triton and Lipofectamine etc. have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Priority

8. Applicant is entitled to the priority date of 11/06/2000 for SEQ ID NO: 2 and 4 based on the disclosure in provisional application number 60/246, 206. Priority date for SEQ ID NO: 4, 6, 8, 10, 12 and 14 will be the instant filing date (11/06/2001).

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9a. Claims 1, 4, 5, 6, 9, 10, 17, 20, 21, 28, 31 and 32 are rejected as being vague and indefinite in the recitation of the term "FGFCX, FCTRX and p35". Abbreviations and acronyms should be spelled out at their first use in the claims for clarity. The protein of interest is described by an arbitrary abbreviation. Claiming biochemical molecules by a particular abbreviated name given to the protein by various workers in the field fails to distinctly claim what that protein is. Claims 2, 3, 7, 8, 11-16, 18, 19, 22-27, 29, 30 and 33-38 are rejected insofar as they depend on rejected claims 1, 6, 17 and 28.

9b. Claim 1 recites the limitation "the at least one cell " in line 2. There is insufficient antecedent basis for this limitation in the claim. Claims 2-5 are rejected insofar as they depend on rejected claim 1.

9c. Claims 1, 6, 17 and 28 are incomplete because methods steps do not refer back to the preamble and relating the steps to the preamble. Claims 2-5, 7, 8, 11-16, 18, 19, 22-27, 29, 30 and 33-38 are rejected insofar as they depend on rejected claims 1, 6, 17 and 28.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10a. Claims 1, 4, 5, 6, 9, 10, 17, 20, 21, 28, 31 and 32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

Claims 1, 4, 5, 6, 9, 10, 17, 20, 21, 28, 31 and 32 recite FGFCX, FCTRX, "a variant of SEQ ID NO: 2 wherein up to 15% of the residues provided in SEQ ID NOs: 2, 4, 6, 8, 10, 12 and 14 are changed according to a conservative amino acid substitution" or "a deletion mutant of SEQ ID NOs: 2, 4, 6, 8, 19, 12 and 14" or "a variant of a deletion mutant of SEQ ID NOs: 2, 4, 6, 8, 19, 12 and 14 wherein up to 15% of the residues provided in the deletion variant are changed according to a conservative amino acid substitution" or "a p35 form of a FCTRX" or "a variant of a p35 form of a FCTRX polypeptide wherein up to 15% of the residues provided in the deletion variant are changed according to a conservative amino acid substitution".

The specification discloses FGF-CX polypeptide with amino acid sequence of SEQ ID NO: 2 and FCTRX polypeptide with amino acid sequence of SEQ ID NOs: 4, 6, 8, 10, 12 and 14 (page 36, Table 13). This disclosure meets the written description provisions of 35 USC 112, first paragraph. However, the instant specification fails to provide adequate written description to the various polypeptides described. Since the instant claims are drawn to methods comprising the polypeptide described above, they lack written description. The claims as written, however, encompass various polypeptide sequences which were not originally contemplated and fail to meet the written description provision of 35 USC 112, first paragraph because the written description is not commensurate in scope with the recitation of claims 1, 4, 5, 6, 9, 10, 17, 20, 21, 28,

31 and 32. The specification does not provide written support for the genus encompassed by the instant claims.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, there is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. The specification does not provide written description to support the genus encompassed by the instant claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (*See Vas-Cath* at page 1116).

With the exception of isolated polypeptide sequences of SEQ ID NOs: 2, 4, 6, 8, 10, 12 and 14 (see page 13, Table 13 of the specification), the skilled artisan cannot envision all the detailed chemical structure of the claimed polypeptide sequences of the variants regardless of the complexity or simplicity of the method of isolation.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what

one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Therefore, only the isolated polypeptide sequences of SEQ ID NO: 2, 4, 6, 8, 10, 12 and 14 but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. As a result, it does not appear that the inventors were in possession of various polypeptide sequences set forth in claims 1, 4, 5, 6, 9, 10, 17, 20, 21, 28, 31 and 32.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

10b. Claims 1, 4, 5, 6, 9, 10, 17, 20, 21, 28, 31 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for FGF-CX polypeptide with amino acid sequence of SEQ ID NO: 2 and FCTRX polypeptide with amino acid sequence of SEQ ID NOs: 4, 6, 8, 10, 12 and 14 (page 36, Table 13), does not reasonably provide enablement for various polypeptides including FGFCX, FCTRX, "a variant of SEQ ID NO: 2 wherein up to 15% of the residues provided in SEQ ID NOs: 2, 4, 6, 8, 10, 12 and 14 are changed according to a conservative amino acid substitution" or "a deletion mutant of SEQ ID NOs: 2, 4, 6, 8, 19, 12 and 14" or "a variant

of a deletion mutant of SEQ ID NOs: 2, 4, 6, 8, 19, 12 and 14 wherein up to 15% of the residues provided in the deletion variant are changed according to a conservative amino acid substitution" or "a p35 form of a FCTRX" or "a variant of a p35 form of a FCTRX polypeptide wherein up to 15% of the residues provided in the deletion variant are changed according to a conservative amino acid substitution". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Claims 1, 4, 5, 6, 9, 10, 17, 20, 21, 28, 31 and 32 are drawn to methods comprising FGFCX, FCTRX, "a variant of SEQ ID NO: 2 wherein up to 15% of the residues provided in SEQ ID NOs: 2, 4, 6, 8, 10, 12 and 14 are changed according to a conservative amino acid substitution" or "a deletion mutant of SEQ ID NOs: 2, 4, 6, 8,

19, 12 and 14" or "a variant of a deletion mutant of SEQ ID NOs: 2, 4, 6, 8, 19, 12 and 14 wherein up to 15% of the residues provided in the deletion variant are changed according to a conservative amino acid substitution" or "a p35 form of a FCTRX" or "a variant of a p35 form of a FCTRX polypeptide wherein up to 15% of the residues provided in the deletion variant are changed according to a conservative amino acid substitution", without any additional structural or functional limitations. The specification defines FGFCX polypeptide with amino acid sequence of SEQ ID NO: 2 and FCTRX polypeptide with amino acid sequence of SEQ ID NOs: 4, 6, 8, 10, 12 and 14 (page 36, Table 13). However, the specification does not provide meaningful structural or functional limitations for all FGFCX polypeptides, FCTRX polypeptides and the variant of these polypeptides.

The specification discloses a human FGFCX polypeptide with amino acid sequence of SEQ ID NO: 2 and FCTRX polypeptide with amino acid sequence of SEQ ID NOs: 4, 6, 8, 10, 12 and 14 (page 36, Table 13). However, the claims are drawn to methods using composition comprising FGFCX, FCTRX, "a variant of SEQ ID NO: 2 wherein up to 15% of the residues provided in SEQ ID NOs: 2, 4, 6, 8, 10, 12 and 14 are changed according to a conservative amino acid substitution" or "a deletion mutant of SEQ ID NOs: 2, 4, 6, 8, 19, 12 and 14" or "a variant of a deletion mutant of SEQ ID NOs: 2, 4, 6, 8, 19, 12 and 14 wherein up to 15% of the residues provided in the deletion variant are changed according to a conservative amino acid substitution" or "a p35 form of a FCTRX" or "a variant of a p35 form of a FCTRX polypeptide wherein up to 15% of the residues provided in the deletion variant are changed according to a

conservative amino acid substitution". None of the modified sequences are presented as working examples. In addition, the specification does not teach structural or functional limitations for the variations of the FGFCX of SEQ ID NO: 2 and FCTRX of SEQ ID Nos: 4, 6, 8, 10, 12 and 14. The usefulness of the methods recited in the claims is tied to the usefulness of the polypeptides. If one skilled in the art is not guided as to how to generate the various polypeptides, then the skilled artisan is also not guided as to how to use methods using the compositions comprising these polypeptides. In the instant application, there is insufficient guidance regarding how to make all FGFCX and FCTRX polypeptide and their variants.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants growth promotion or treating an inflammatory pathology or other functional attributes of the instant polypeptide. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. Therefore, predicting which polypeptide(s), if any, would retain the functions of the protein is well outside the realm of routine experimentation. Thus, an undue amount of experimentation would be required to generate the changes/modifications contemplated and yet retain the function of the proteins claimed.

Applicant has not taught how one of skilled in the art would use the full scope of polypeptide sequences encompassed by the invention of claims 1, 4, 5, 6, 9, 10, 17, 20, 21, 28, 31 and 32 -20. The specification as filed does not sufficiently teach one of skilled in the art how to make and/or use the full scope of the claimed sequences. The amount

of experimentation required to make and/or use the full scope of the claimed sequences would require trial and error experimentation to determine the functional sequences.

Given the breadth of claims 1, 4, 5, 6, 9, 10, 17, 20, 21, 28, 31 and 32 in light of the unpredictability of the art as determined by the lack of working examples and as shown by the prior at of record, the level of skill of the artisan, and the lack of guidance provided in the instant specification, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

10c. Claims 6-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of treatment of a subject with inflammatory bowel disease, specifically Colitis and Crohn's disease by administering a composition comprising a combination of FGFCX polypeptide of SEQ ID NO: 2 and FCTRX polypeptide of SEQ IDNO: 4 or 6, the specification does not reasonably provide enablement for the method of treatment or method of delaying the onset or a method of ameliorating a subject suffering with non gastro inflammatory pathology by administering a composition comprising combination of all FGFCX polypeptides and all FCTRX polypeptides or variants of these polypeptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 6-38 are drawn to the method of treatment or method of delaying the onset or a method of ameliorating or a method of reducing the mortality or a method of delaying the mortality of a subject with inflammatory pathology in general (includes both

non-gastrointestinal and intestinal) by administering a composition comprising combination of all FGFCX polypeptides and all FCTRX polypeptides or the variants of these polypeptides. However, Applicants have demonstrated using various mouse and rat models (see examples 26-29) potential treatment by administering FGFCX of SEQ ID NO: 2 or FCTRX of SEQ ID NO: 4 or 6 comprising compositions for inflammatory bowel disease (IBD) only, including Colitis and Crohn's disease which cause gastrointestinal pathology induced by sodium dextran sulfate. However, the specification as filed is insufficient to enable one skilled in the art to practice the claimed invention without an undue amount of experimentation because inflammatory pathology could be the result of several diseases that are caused by various etiologies. In addition, the inflammatory bowel diseases taught in the specification are limited to gastrointestinal tract, yet the scope of the claims encompasses all inflammatory pathology of the subject. Inflammatory pathology is associated various diseases including with transplant tissue rejection (graft-versus-host-disease), psoriasis, periodontitis, asthma, multiple sclerosis and others, yet the specification describes the treatment of inflammatory pathology associated with gastrointestinal in examples 26-29. In fact, Applicants own work published post filing (Jeffers et al. 2002) of the instant Application is also limited to the treatment on intestinal inflammation by FGF-20 (FGFCX). The usefulness of the methods of treatment recited in the claims is tied to the usefulness of FGFCX of SEQ ID NO: 2 and FCTRX of SEQ ID NO: 4 and 6 in treating inflammatory pathology associated with the gastrointestinal tract. Since, the above-mentioned diseases and others are not known in art to have inflammatory pathology

associated with the gastrointestinal tract, it is unclear how one skilled in the can extrapolate the observations to treat diseases with inflammatory pathology not associated with the gastrointestinal tract by administering a composition comprising combination of all FGFCX polypeptides and all FCTRX polypeptides or the variants of these polypeptides. If one skilled in the art is not guided as to the pathology of the various diseases, then the skilled artisan is also not guided as to how to use methods for the treatment using the compositions comprising these polypeptides. Since, there is inadequate guidance as to the nature of the invention is provided, it is merely an invitation to the artisan to use the current invention as a starting point for further experimentation to try various diseases with inflammatory pathology not associated with the gastrointestinal tract. In addition, because there are no working examples provided describing diseases or models with inflammatory pathology not associated with the gastrointestinal it would require an undue amount of experimentation to one of skill in the art to practice the claimed invention.

In addition, there is no guidance provided for the mechanism associated with the inflammatory pathology recited in the claims. While mechanism is not required, it can allow extrapolation of enablement to non-exemplified embodiments. Since applicant has not provided any working examples to teach the method of treatment or method of delaying the onset or a method of ameliorating or a method of reducing the mortality or a method of delaying the mortality of a subject suffering with non-gastrointestinal inflammatory pathology by administering a composition comprising combination of all FGFCX polypeptides and all FCTRX polypeptides or the variants of these polypeptides

either *in vitro* or *in vivo*, it would require an undue amount of experimentation to one of skill in the art to practice the invention commensurate in scope with the claims to treat all diseases with inflammatory pathology.

Given the breadth of claims 6-38 in light of the unpredictability of the art as determined by the lack of working examples, the level of skill of the artisan, and the lack of guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention for a method of treatment or method of delaying the onset or a method of ameliorating or a method of reducing the mortality or a method of delaying the mortality of a subject suffering with inflammatory pathology by administering a composition comprising combination of all FGFCX polypeptides and all FCTRX polypeptides or the variants of these polypeptides.

10d. Claims 1- 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of promoting the growth of intestinal epithelial cells, colonic cells, NIH 3T3 cells, human primary osteoblast cells and pulmonary artery smooth muscle cells by contacting the cells with a composition comprising a combination of FGFCX polypeptide of SEQ ID NO: 2 and FCTRX polypeptide of SEQ ID NO: 4 and 6, the specification does not reasonably provide enablement for the method of promoting the growth of a population of cells comprising contacting at least one cell with a composition, comprising a polypeptide, wherein a composition comprises a combination of all FGFCX polypeptides and all FCTRX polypeptides or the variants of these polypeptides in the instant invention. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-5 are drawn to the method of promoting the growth of a population of cells comprising contacting at least one cell with a composition comprising a combination of all FGFCX polypeptides and all FCTRX polypeptides or variants of these polypeptides. However, Applicants have demonstrated using various *in vitro* and *in vivo* models (see examples 26-29) promoting the growth of intestinal cells comprising contacting at least one cell with a composition, comprising a combination of FGFCX polypeptide of SEQ ID NO: 2 and FCTRX polypeptide of SEQ ID NO: 4 or 6. However, the specification as filed is insufficient to enable one skilled in the art to practice the claimed invention without an undue amount of experimentation because there is no evidence to suggest that FGF-20 will promote the growth of all cells upon contact. In addition, the art teaches that different FGF polypeptides promote the growth of different tissue cells. For example, FGF17 and FGF8 have been demonstrated cooperate to regulate neuroepithelial proliferation in the midbrain-hindbrain junction (see Ornitz et al., (2001)). Applicants own work published post filing (Jeffers et al. 2002) of the instant Application is also limited to the intestinal cell growth following FGF-20 (SEQ ID NO: 2) contact. The usefulness of the present methods recited in the claims is tied to the usefulness of polypeptide comprising a combination of FGFCX polypeptide of SEQ ID NO: 2 and FCTRX polypeptide of SEQ IDNO: 4 or 6 in promoting cell growth in the gastrointestinal tract (epithelial cells). Since, the above-mentioned polypeptide is not

known in the art to have growth promoting capabilities all cells, it is unclear how one skilled in the art can extrapolate the observations of the instant invention to promote cells growth not associated with the gastrointestinal tract with the polypeptide composition of the instant invention.

If one skilled in the art is not guided as to the abilities of the combination of FGFCX polypeptide of SEQ ID NO: 2 and FCTRX polypeptide of SEQ ID NO: 4 or 6 to promote the growth of various cell types, then the skilled artisan is also not guided as to how to use methods for promoting the growth of a population of cells using the compositions comprising these polypeptides. Since, there is inadequate guidance as to the nature of the invention, it is merely an invitation to the artisan to use the current invention as a starting point for further experimentation to try the growth of various cell populations not associated with the gastrointestinal tract. In addition, because there are no working examples provided describing the cell populations not associated with the gastrointestinal it would require an undue amount of experimentation to one of skill in the art to practice the claimed invention.

Given the breadth of claims 1- 5 in light of the unpredictability of the art as determined by the lack of working examples, the level of skill of the artisan, and the lack of guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention for a method of promoting the growth of a population of cells by contacting at least one cell with a composition comprising a combination of FGFCX polypeptide of SEQ ID NO: 2 and FCTRX polypeptide of SEQ I DNO: 4 or 6

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11a. Claims 6-16 and 28-36 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 and 11-26 of U.S. Patent No. 6, 982,250. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant invention is directed to a method of treating an inflammatory pathology or a method of ameliorating of a subject with inflammatory pathology in general (includes both non-gastrointestinal and intestinal) by administering a composition comprising a combination of a FGFCX polypeptide (SEQ ID NO: 2) and a FCTRX polypeptide (SEQ ID NO: 4, 6, 8, 10, 12 and 14) compared to those described in U.S. Patent No. 6, 982,250 that is directed to treating method using a polypeptide comprising SEQ ID NO: 2. The comprising

language does not preclude the use of other polypeptides in the composition. In fact the Lichenstein et al. reference does teach use of both FGFCX polypeptide and FCTRX polypeptide in the methods (column 1, line 60-61). In addition, claims of the instant invention describe methods of treating an inflammatory pathology, which also encompasses inflammatory bowel diseases disclosed in the allowed patent. Therefore, claims 6-16 and 28-38 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 and 11-26 of U.S. Patent No. 6, 982,250.

11b. Claims 1-38 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims1-3, 5, 6-8, 19, 21-30 and 32-38 of copending Application No. 10/321,962. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant invention is directed to method of promoting the growth of a population of cells or a method of delaying the onset of an inflammatory pathology or a method of treatment of an inflammatory pathology or a method of ameliorating of a subject with inflammatory pathology in general (includes both non-gastrointestinal and intestinal) by administering a composition comprising a combination of a FGFCX polypeptide and a FCTRX polypeptide compared to those described in U.S. Patent No. 7, 189, 693 that is directed methods using a polypeptide comprising amino acids 24-211 of SEQ ID NO: 2 (FGFCX). The comprising language does not preclude the use of other polypeptides in the composition. The dependent claims in fact recite the combination of

FCTRX polypeptides (SEQ ID NO: 4, 6, 8, 10, 12 and 14). In addition, claims of the instant invention describe methods of treating an inflammatory pathology, which also encompasses inflammatory bowel diseases disclosed in the allowed patent. Therefore, claims 1-38 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims1-3, 5, 6-8, 19, 21-30 and 32-38 of copending Application No. 10/321, 962.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

12. No Claims are allowable.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon, Ph.D whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Gagatheesa Scheslay
Patent Examiner

JS
Art Unit 1647
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